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ORIGINAL ARTICLE

The Use of Stem Cells in Dental Implant Site Development

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ABSTRACT

Aim: The use of stem cells in dental implant site development
Methods: A total of 15 patients were enrolled and divided into three groups, with each group receiving $1x10^5$, $1x10^6$, and $1x10^7$ stem cell treatment dosages. Following treatment, CT scan was done to measure their bone mineral density (BMD), which was scored using Hounsfield units (HU) grading. Tests were performed prior to treatment, as well as 4,6,8,12 weeks after dental implantation to determine the success of the procedure.
Results: There were no major side effects over the six-month study period. There was no association identified between the stem cell transplant and any of the side effects Multiplex immunological tests were used to determine the amount of cytokines and chemokines present in the subjects. The inflammatory markers eotaxin, FGF2, MCP-1, MDC, and IL17a were elevated in patients treated with stem cells. Stem cells secrete cytokines and chemokines that aid in the healing of damaged tissue.
Conclusions: Stem cell treatment for dental implantation is well tolerated and has no significant negative effects.
Keywords: Stem cell, dental implantation

INTRODUCTION

The success of dental implant surgery is highly dependent on the integrity of the surrounding bone[1]. When teeth are extracted, guided bone regeneration (GBR) is a frequent procedure used to improve the osseointegration of the alveolar bone that surrounds the tooth extraction site. In addition to boosting osteogenesis and osteoconduction, the GBR treatment helps to stimulate bone formation by utilizing a barrier membrane to keep non-osteogenic tissue out of the treatment area.

The use of stem cells to increase GBR has also been promoted as a method of increasing GBR.

METHODOLOGY

As part of a "5 + 5 design," we used sequential cohorts in clinical trial to determine the appropriate sample size for analysis. A "5 +5 design," to put it simply, entails enrolling five patients at a low dose at the start of the research. In order to establish the safety profile, a total of 15 patients had to be included. A low dose ($1x10^5$ CD61Lin cells/0.25ml DPBS) was administered to the first five patients; a medium dose ($1x10^6$ CD61Lin cells/0.25 ml DPBS) to other five patients; a high dose ($1x10^7$ CD61Lin cells/0.25 ml DPBS) to the last five patients. BMD was measured every week for 24 weeks during this study. Hard tissue examinations were performed weekly basis for the next 24 weeks following GBR: weeks 1, 2, 8, 12, 16, 18, and 20.

Inclusion Criteria: Age at least 20 years, **t**he opposing dentition is natural teeth, fixed crowns on natural teeth, or bridges on natural teeth, **t**he subject has one missing maxillary or mandibular posterior tooth that necessitates an alveolar bone replacement procedure before a dental implant can be placed and no removable prostheses or dentures are allowed.

CD61LIN SB cells purification: 40 ml of blood was collected and placed in four tubes of EDTA. The blood samples were separated into two layers 48–72 hours after they were acquired. After the top layer was removed, the SB mixture was pipetted into a 50 ml tube and centrifuged for 15 minutes and then washed with 10 ml DPBS before being transferred into 15mm tubes for extraction. To eliminate mature hematopoietic cells from the SB mixture, we employed a Miltenyi Biotec human lineage depletion kit, and anti-CD61 antibody-coated micro beads were used to remove CD61+ cells. Cell size and the Lgr5+ population in CD61Lin SB cells were measured using flow cytometry on CD61Lin SB cells. The CD61Lin SB cell product was evaluated in accordance with the following criteria:

- The tests for mycoplasma and fungal sterility And tests for cell viability, endotoxin, and Lgr5+ cell counts, all came out negative.
- 80% of the cells were viable, and cell numbers were <2.5%
- The diameter of the cells 2 and 5 mm.
- The CD61Lin SB cell product was diluted in 0.25 ml of DPBS

After the SB cells were injected, an absorbable double-layer collagen membrane was utilized to cover the wound. An entire thickness flap was created on the surgical site under local anesthesia. The GBR collagen complex was applied. A second treatment was performed following the removal of the granulation tissue. SB cells and hydroxyl apatite powder were used to fill the alveolar bone deficits, and repeated a third time. It was necessary to stitch the area around the wound after the absorbable collagen membrane had been applied. The Osseotite® acid-etched implants were placed 12 weeks following the GBR operation. To compare the overall responses of the three dose groups, one-way ANOVA and Tukey's post hoc analysis were employed in conjunction with each other. SPSS version 25 was used.

RESULTS

Table 1: Clinical Characteristics

#	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Age	64	72	44	29	54	57	80	49	45	60	69	59	70	53	48
Sex	F	M	M	M	F	M	F	M	M	M	F	F	M	M	M
Dose (CD61-lin-SB cells	Low ($1x10^5$)	Low ($1x10^5$)	Low ($1x10^5$)	Low ($1x10^5$)	Low ($1x10^5$)	Medium ($1x10^6$)	Medium ($1x10^6$)	Medium ($1x10^6$)	Medium ($1x10^6$)	Medium ($1x10^6$)	High ($1x10^7$)	High ($1x10^7$)	High ($1x10^7$)	High ($1x10^7$)	High ($1x10^7$)
Missing tooth	15	14	47	35	46	26	37	36	36	46	35	16	15	47	34

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Table 2: Density of bone mineral in patients

Visit	Follow up	Cases (HU)														
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1	Screening	330	170	198	207	405	252	201	129	360	167	191	211	424	251	221
3	GBR	330	443	224	247	475	243	280	490	391	439	222	256	478	242	284
4	1 week after GBR	328	571	277	251	481	393	550	697	398	564	275	254	489	396	559
5	2 week after GBR	400	636	354	309	481	391	616	597	408	634	352	314	499	399	618
7	8 week after GBR	411	892	561	422	489	460	555	717	418	871	564	419	489	455	558
8	12 week after GBR	598	1094	745	550	1158	1542	839	907	598	1099	746	543	1162	1546	845
10	4 week after implantation	756	1773	942	915	1547	1004	939	717	759	1756	941	903	1557	1001	947
11	6 week after implantation	833	1887	935	1184	1609	1017	954	999	877	1886	933	1177	1617	1019	954
12	8 week after implantation	946	2410	1183	1293	1746	983	1224	1853	950	2408	1182	1282	1744	982	1224
13	12 week after implantation	1057	2622	1375	1893	1820	1050	1124	1982	1068	2544	1379	1873	1839	1054	1474

DISCUSSION

According to the findings, all the patients had good outcomes. Counting down from one to four, the success of dental implants in osseointegration is reliant on a variety of parameters. A substantial influence is played by both trabecular bone density and cortical bone density when it comes to promoting bone regeneration and implant durability. As a result, measures of bone mineral density and maximum stress may be able to capture some of the treatment-induced changes in bone quality and quantity. The larger mean trabecular non-cortical bone density, also known as the D2–D3 level of bone density, was assessed in this study to determine whether or not the posterior mandible possessed this level of bone density. Implant patients were assigned density levels in the D3 range, which is relevant because higher density levels have been linked to worse implant success rates in the past. Adding more research, such as a biopsy of the cortical bone thickness or an evaluation of the microarchitecture of trabecular bones, could have improved the conclusions of the study [2,4].

Following the completion of this experiment, it was discovered that SB cells were a safe and effective treatment option for treating human patients who had significant alveolar bone abnormalities. In addition to implant insertion, the safety and tolerability trials presented here may also be applicable to other oral treatments that necessitate the rapid remineralization of bone, such as root canal therapy.

SB cells do not worsen the systemic inflammatory response, according to the results of cytokine and chemokine assays, and can therefore be employed safely in localized applications without risk of infection. Even though statistically significant changes in the majority of cytokines and chemokines were not discovered between the stipulated time periods in all groups, six biomarkers (Fracktalk, IL-17A, FGF2, eotaxin, MDC, and MCP-1) exhibited a consistent trend across the 24-week investigation. As a result of these observations, it was determined that SB cells possess immunomodulatory capabilities that have an effect on the immune system. The results of the study reveal that FGF2 can increase vascularization and speed up physiological bone regeneration in the intermediate and high dose groups, according to the findings. This process has been shown to be influenced by the chemokines eotaxin, MDC, and MCP-1.

MCP-1 levels increased more rapidly with greater dosages, but there was a general dose-dependent effect in all groups, regardless of the amount used. Only patient 2 had considerably lower MCP-1 protein expression than the other patients. In light of these encouraging findings, it is possible that MCP-1 will be employed as a surrogate marker for SB cells in future studies. It is known as a receptor ligand when MCP-1 (also known as CCL2) interacts with the CCR2 (also known as the Duffy antigen receptor). According to this investigation, increased levels of MCP-1 may be associated with bone regeneration. It has been demonstrated that many stem cell sources can mobilize calcium, aid in bone growth and healing, and improve bone formation and wound healing in a variety of settings[5,6,7].

CONCLUSION

SB cells were safe and acceptable in patients with significant bone abnormalities. Furthermore, SB cells appeared to have speed up the process of tooth repair. SB cells have the potential to stimulate bone regeneration.

Conflict of interest: Mil

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